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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,706	12/11/2003	James E. Hagstrom	Mirus.048.01	8647

7590
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06/02/2005

EXAMINER

KAUSHAL, SUMESH

ART UNIT PAPER NUMBER

1636

DATE MAILED: 06/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/733,706

Applicant(s)

HAGSTROM ET AL.

Examiner

Sumesh Kaushal Ph.D.

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 March 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9,11-13,15 and 16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9,11-13,15 and 16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's response filed on 3/14/05 has been acknowledged.

Claims 10, 14 and 17 are canceled.

Claims 1-9, 11-13 and 15-16 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 1-9 and 11-13 and 15-16 stand rejected under 35 U.S.C. 102(b) as being anticipated by Stedman et al (WO 99/31982, 1999) for the same reasons of record as set forth in the office action mailed on 01/21/05.

The instant claims are drawn to a method for delivering polynucleotide to extra vascular parenchymal cell in a limb of a mammal in-vivo by inserting a viral vector in large volume into the lumen of vessel.

Response to Arguments

Applicant's arguments filed on pages 4-5 regarding prior art issues have been fully considered but they are not persuasive. The applicant argues that the for delivery of adenovirus to limb muscle cells, the method of Stedman requires either injection of both histamine and papaverine or, perfusion of the limb with a solution containing either a vascular permeability enhancing agent or a vasodilating agent for 45 minutes under pressure followed by removal and flush of the injection solution. The applicant argues that the perfusion requires accessing both an artery and a vein and circulating fluid though the limb using a pump The applicant argues that the in contrast, applicant's

process requires only injection of fluid containing the virus into a limb artery or vein and does not require injection of a vascular permeability enhancing agent or a vasodilating agent and permits blood flow to the limb to be restored within 2 minutes of injection of the virus. The applicant argues that the Stedman does not teach injection of a viral vector in a large volume. The applicant argues that the applicants submit, a declaration under 37 CFR 1.132 showing delivery of adeno- associated virus to limb skeletal muscle cells in mouse and rat without injection of either papaverine or histamine or other vasodilating compound.

The applicant argues that even though Stedman teaches increasing vessel permeability by providing virus vector suspension continuously at high pressure, it is the applicant's understanding that Stedman injects virus in a low volume followed by injection of a chase volume and perfusion under pressure. The applicant argues that it is recognized that the greater the increase in perfusion pressure, the greater is the risk of structural damage to vascular and extravascular tissues. The applicant argues that the applicants method increases volume/pressure in the mammal through injection of a solution containing the virus, does not require perfusion, and does result in delivery of virus to extravascular cells.

However, applicant's arguments are found not persuasive because the invention as claimed requires delivering polynucleotide to extra vascular parenchymal cells in a limb by inserting a viral vector in large volume into the lumen of vessel to force the injected fluid out of the vasculature and into the extravascular space which is clearly anticipated by cited prior art of record, given the broadest reasonable interpretation. Stedman clearly teaches transvascular delivery of a composition comprising a viral vector to an extravascular tissue of a mammal. The cited art teaches the transport of an adenovirus vector from the lumen of vascular capillaries to the interstitium of muscle tissue (page 53 example-1). The cited art teaches delivery of a viral vector through an artery or a vein (example -1, pages 54-56). The declaration provided under 37 CFR 1.132 has been fully considered. However, applicants arguments regarding the use of vascular permeability agents has found unpersuasive, since applicant argues about the negative claim limitation that has not been recited in the instant claims.

Furthermore contrary applicant's assertion, claims 12 and 16 clearly recites injecting "vasodilator", which has been clearly anticipated by cited art of record. For example the cited art clearly teaches increasing vascular permeability using permeability-enhancing agent is selected from the group consisting of histamine, acetylcholine, an adenosine nucleotide, arachidonic acid, bradykinin, cyanide, endothelin, endotoxin, interleukin-2, ionophore A23 187, nitroprusside, a leukotriene, an oxygen radical, phospholipase, platelet activating factor, protamine, serotonin, tumor necrosis factor, vascular endothelial growth factor, a venom, and a vasoactive amine (page 8, lines 18-28, page 9, lines 1-16, page 20, page 63 example-2). Even though Stedman teaches increasing vessel permeability by providing virus vector in a low volume followed by injection of a chase volume and perfusion under pressure, such a teaching clearly anticipate the invention as claimed that merely requires inserting viral vector in large volumes. Furthermore, as argued by the applicant the administration of vector is not limited to 45 minutes. In addition rapid injection of a large volume would inherently results in an increase in pressure along with some risk of structural damage to vascular and extravascular tissues. Thus given the broadest reasonable interpretation to the invention as claimed the cited art clearly anticipate the invention as claimed.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of


the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547**. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**.

Sumesh Kaushal
Examiner GAU 1636



SUMESH KAUSHAL
PATENT EXAMINER